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(54) Title: METHODS OF PRODUCING OR IDENTIFYING INTRABODIES IN EUKARYOTIC CELLS

(57) Abstract: The present invention relates to a high efficiency method of expressing intracellular immunoglobulin molecules in eukaryotic cells. The invention is further drawn to a method of producing intracellular immunoglobulin libraries, particularly using the trimolecular recombination method, for expression in eukaryotic cells. The invention further provides methods of selecting and screening for intracellular immunoglobulin molecules and fragments thereof. The invention also provides kits for producing, screening and selecting intracellular immunoglobulin molecules. Finally, the invention provides intracellular immunoglobulin molecules and fragments thereof, produced by the methods provided herein.

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What Is Claimed Is:

1. A method of selecting polynucleotides which encode an intracellular immunoglobulin molecule, or fragment thereof, whose expression induces a modified phenotype in a eukaryotic host cell, comprising:

5 (a) providing a population of eukaryotic host cells capable of expressing said intracellular immunoglobulin molecule, or fragment thereof, wherein individual host cells of said population can be induced to exhibit a predetermined modified phenotype;

10 (b) introducing into said population of host cells a first library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of first intracellular immunoglobulin subunit polypeptides, each comprising a first immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region;

15 (c) introducing into said population of host cells a second library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of second intracellular immunoglobulin subunit polypeptides, each comprising a second immunoglobulin variable region selected from the group consisting of a heavy chain variable region and a light chain variable region, wherein said second immunoglobulin variable region is not
20 the same as said first immunoglobulin variable region, and wherein said second intracellular immunoglobulin subunit polypeptides combine with said first intracellular immunoglobulin subunit polypeptides to form a plurality of intracellular immunoglobulin molecules, or fragments thereof;

25 (d) permitting expression of said plurality of intracellular immunoglobulin molecules, or fragments thereof in said population of host cells under conditions wherein said modified phenotype can be detected; and